510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

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Trade Name: Access HIV Ag/Ab combo, Access HIV Ag/Ab combo Calibrators, & Access HIV Ag/Ab combo QC
Common Name: HIV Serological Detection Test System
Classification Regulation: 21 CFR 866.3956; 862.1150; 862.1660
Classification Product Code*:* MZF, JIT, MJY, MJX, MJZ

Predicate Device:
Abbott ARCHITECT™ HIV Ag/Ab Combo, BP090080

Device Description

The Access HIV Ag/Ab combo assay requires Access HIV Ag/Ab combo (reagent packs), Access HIV Ag/Ab combo Calibrators (C1 and C2), and Access HIV Ag/Ab combo QC (QC1-QC5). The assay for HIV-1 p24 antigen detection (HIV-Ag) is a one-step immunoenzymatic “sandwich” assay. Paramagnetic particles (PMP) coated with recombinant anti-HIV-1 p24 antibody, paramagnetic particles coated with three HIV peptides representing HIV-1 group M, HIV-1 group O and HIV-2 antigens, monoclonal anti-HIV-1 p24 antibody conjugated to alkaline phosphatase (ALP), and sample are added to a reaction vessel. HIV-1 p24 present in the patient sample is bound in a “sandwich” complex between the anti-HIV-1 p24 antibody coated on the solid phase and the anti-HIV-1 p24 antibody conjugate. After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. A chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is compared to the HIV-1 p24 antigen cutoff value defined during calibration of the instrument. Qualitative assessment of HIV-1 p24 antigen is automatically determined from a stored calibration.

The assay for anti-HIV-1 / anti-HIV-2 antibody (HIV-Ab) Detection is a two-step immunoenzymatic "sandwich" assay. Paramagnetic particles coated with recombinant anti-HIV-1 p24 antibody, paramagnetic particles coated with three HIV peptides representing HIV-1 group M, HIV-1 group O and HIV-2 antigens, monoclonal anti-tag antibody conjugated to alkaline phosphatase, three tagged HIV peptides representing HIV-1 group M, HIV-1 group O and HIV-2 antigens, and sample are added to a reaction vessel. Antibodies to HIV-1 group M, HIV-1 group O or HIV-2 present in the patient sample are bound in a "sandwich" complex between the HIV peptides coated on the solid phase and the tagged HIV peptides/anti-tag conjugate. After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. The same three tagged HIV peptides and monoclonal anti-tag antibody conjugated to alkaline phosphatase (OVL- overload) are added to the reaction vessel and incubated. After this second incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. A chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is compared to the antibody cutoff value defined during calibration of the instrument. Qualitative assessment of HIV antibodies is automatically determined from a stored calibration.

The Access HIV Ag/Ab combo Calibrators are used to establish calibration (determine the cutoff value) for the Access HIV Ag/Ab combo assay. By comparing the light intensity generated by a sample to the cutoff value, the presence or absence of human immunodeficiency virus antigen and/or antibodies in the sample is determined. Two calibrators are used with Access HIV Ag/Ab combo assay. Calibrator C1 is dedicated to the Ag analysis, while Calibrator C2 is dedicated to the Ab analysis.

Quality control (QC) materials simulate the characteristics of patient samples and are essential for monitoring the system performance of the Access HIV Ag/Ab combo immunoassays. In addition, they are an integral part of good laboratory practices.

The Access HIV Ag/Ab combo reagents are provided in liquid ready-to-use format designed for optimal performance on the Beckman Coulter DxI 9000 Access Immunoassay Analyzer only. Each reagent kit contains two reagent packs. The calibrator kit and QC kit contain one vial per level. Other items needed to run the assay include Lumi-Phos PRO substrate and UniCel DxI Wash Buffer II.

Intended Use

The Access HIV Ag/Ab combo assay is a paramagnetic particle, chemiluminescent immunoassay for the simultaneous qualitative in vitro detection and differentiation of HIV-1 p24 antigen and antibodies to HIV-1 (groups M and O) and/or HIV-2 in human pediatric (ages 2 through 21 years) and adult serum and serum separator tubes or plasma [lithium heparin, lithium heparin separator tubes, dipotassium (K_2) EDTA, tripotassium (K_3) EDTA, sodium citrate, acid-citrate-dextrose (ACD) and citrate phosphate-dextrose (CPD)] using the DxI 9000 Access Immunoassay Analyzer.

The Access HIV Ag/Ab combo assay is intended to be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection, including acute or primary HIV-1 infection. The assay may also be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection in pregnant women.

The Access HIV Ag/Ab combo assay is for use on the DxI 9000 Access Immunoassay Analyzer only.

This assay is not intended for use for screening donors of blood or blood products or human cells, tissues, or cellular or tissue-based products (HCT/Ps).

The Access HIV Ag/Ab combo Calibrators are intended to calibrate the Access HIV Ag/Ab combo assay for the simultaneous qualitative detection and differentiation of HIV-1 p24 antigen and antibodies to HIV-1 (groups M and O) and/or HIV-2 in human serum and plasma, using the DxI 9000 Access Immunoassay Analyzer.

The Access HIV Ag/Ab combo QC is intended for monitoring system performance of the Access HIV Ag/Ab combo assay. The Access HIV Ag/Ab combo QC is for use on the DxI 9000 Access Immunoassay Analyzer.

Comparison Table

Features / Characteristics	**Candidate Device** Access HIV Ag/Ab combo	**Predicate Device (BP090080)** ARCHITECT HIV Ag/Ab Combo	**Comment**
Reagent Intended Use and **Clinical Indications**	The Access HIV Ag/Ab combo assay is a paramagnetic particle, chemiluminescent immunoassay for the simultaneous qualitative *in vitro* detection and differentiation of HIV-1 p24 antigen and antibodies to HIV-1 (groups M and O) and/or HIV-2 in human pediatric (ages 2 through 21 years) and adult serum and serum separator tubes or plasma [lithium heparin, lithium heparin separator tubes, dipotassium (K_2) EDTA, tripotassium (K_3) EDTA, sodium citrate, acid-citrate-dextrose (ACD) and citrate phosphate-dextrose (CPD)] using the DxI 9000 Access Immunoassay Analyzer. **The Access HIV Ag/Ab combo assay is intended to be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection, including acute or primary HIV-1 infection. The assay may also be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection in pregnant women.** The Access HIV Ag/Ab combo assay is for use on the DxI 9000 Access Immunoassay Analyzer only. This assay is not intended for use for screening donors of blood or blood products or human cells, tissues, or cellular or tissue-based products (HCT/Ps).	The ARCHITECT HIV Ag/Ab Combo assay is a chemiluminescent microparticle immunoassay (CMIA) for the simultaneous qualitative detection of human immunodeficiency virus (HIV) p24 antigen and antibodies to HIV type 1 (HIV-1 group M and group O) and/or type 2 (HIV-2) in human serum and plasma (EDTA and heparin). **The ARCHITECT HIV Ag/Ab Combo assay is intended to be used as an aid in the diagnosis of HIV-1/HIV-2 infection, including acute or primary HIV-1 infection. The assay may also be used as an aid in the diagnosis of HIV-1/HIV-2 infection in pediatric subjects (*i.e.*, children as young as two years of age) and in pregnant women.** An ARCHITECT HIV Ag/Ab Combo reactive result does not distinguish between the detection of HIV-1 p24 antigen, HIV-1 antibody, or HIV-2 antibody. The ARCHITECT HIV Ag/Ab Combo assay is not intended for use in screening blood or plasma donors. The effectiveness of ARCHITECT HIV Ag/Ab Combo for use in screening blood or plasma donors has not been established. However, this assay can be used as a blood donor screening assay in urgent situations where traditional licensed blood donor screening tests are unavailable or their use is impractical.	Similar

Features / Characteristics	**Candidate Device** Access HIV Ag/Ab combo	**Predicate Device (BP090080)** ARCHITECT HIV Ag/Ab Combo	**Comment**
Calibrator Intended Use	The Access HIV Ag/Ab combo Calibrators are intended to calibrate the Access HIV Ag/Ab combo assay for the simultaneous qualitative detection and differentiation of HIV-1 p24 antigen and antibodies to HIV-1 (groups M and O) and/or HIV-2 in human serum and plasma, using the DxI 9000 Access Immunoassay Analyzer.	The ARCHITECT HIV Ag/Ab Combo Calibrator (CAL 1) is for the calibration of the ARCHITECT *i* System when the system is used for the simultaneous qualitative detection of human immunodeficiency virus (HIV) p24 antigen and antibodies to HIV type 1 (HIV-1 group M and group O) and/or type 2 (HIV-2) in human serum or plasma using the ARCHITECT HIV Ag/Ab Combo assay. The performance of the ARCHITECT HIV Ag/Ab Combo Calibrator has not been established with any other HIV assay.	Similar
QC Intended Use	The Access HIV Ag/Ab combo QC is intended for monitoring system performance of the Access HIV Ag/Ab combo assay. The Access HIV Ag/Ab combo QC is for use on the DxI 9000 Access Immunoassay Analyzer.	The ARCHITECT HIV Ag/Ab Combo Controls (CONTROL –, CONTROL + 1, CONTROL + 2, CONTROL + 3, CONTROL + 4) are used for monitoring the performance of the ARCHITECT *i* System (reagents, calibrator, and instrument) when used for the simultaneous qualitative detection of human immunodeficiency virus (HIV) p24 antigen and antibodies to HIV type 1 (HIV-1 group M and group O) and/or type 2 (HIV-2) in human serum or plasma using the ARCHITECT HIV Ag/Ab Combo assay.	Similar
Environment of Use	Health Care Providers requesting samples to be tested by clinical laboratory technicians	Same	N/A
Operating Principle	Sandwich immunoassay technology	Same	N/A
Analyte Measured	HIV-1 p24 antigen and antibodies to HIV-1 (groups M and O) and/or HIV-2	Same	N/A
Antibody and Antigen sources	Monoclonal (mouse) anti-tag antibody Monoclonal (mouse) anti-HIV-1 p24 antibody Histamine tagged HIV peptides representing HIV-1 group M, HIV-1 group O and HIV-2 antigens	Acridinium-labeled HIV-1 antigens, acridinium-labeled HIV-1/HIV-2 synthetic peptides, and acridinium-labeled HIV p24 antibody (mouse IgG, monoclonal)	Different
Assay Type	HIV-1 p24 antigen detection (HIV-Ag) Assay type: one-step immunoenzymatic “sandwich” assay Anti-HIV-1 / anti-HIV-2 antibody detection (HIV-Ab) Assay type: two-step immunoenzymatic “sandwich” assay	Two-step immunoassay to determine the presence of HIV-1 p24 antigen, antibodies to HIV-1 (group M and group O), and antibodies to HIV-2	Different
Detection Method	Automated, Chemiluminescence	Same	N/A
Reagent, Calibrator, and QC format	Liquid, ready to use	Same	N/A
Calibrator(s)	2	1	Different

Features / Characteristics	**Candidate Device** Access HIV Ag/Ab combo	**Predicate Device (BP090080)** ARCHITECT HIV Ag/Ab Combo	**Comment**
Standardization	HIV-1 p24 antigen detection (HIV-Ag) has been standardized against the WHO International Standard HIV-1 p24 Antigen, NIBSC (National Institute for Biological Standards and Control) code 90/636.	The ARCHITECT HIV Ag/Ab Combo Calibrator 1 is standardized to the Agence française de sécurité sanitaire des produits de santé (AFSSAPS) HIV-1 p24 antigen 50 pg/mL international standard.	Different
Traceability	The Access HIV Ag/Ab combo Calibrator (C1) is traceable to manufacturer's internal reference materials. There is no internationally recognized standard for HIV-1 or HIV-2 specific antibody. The Access HIV Ag/Ab combo Calibrator (C2) is traceable to the manufacturer's internal reference materials. Traceability process is based on EN ISO 17511.	Unknown	Different
Sample Type	Serum and Plasma	Same	N/A
Compatible Anticoagulants	Serum Serum and serum separator tube Plasma Lithium Heparin Lithium Heparin separator tube Dipotassium (K_2) EDTA Tripotassium (K_3) EDTA Sodium Citrate Acid Citrate Dextrose (ACD) Citrate Phosphate Dextrose (CPD)	Serum Serum and serum separator tube Plasma Lithium Heparin with gel separator Sodium heparin Dipotassium (K_2) EDTA Dipotassium (K_2) EDTA with gel separator Tripotassium (K_3) EDTA Disodium (Na_2) EDTA	Different
Sample Volume	60 µL	150 µL	Different
Instrumentation	DxI 9000 Access Immunoassay Analyzer	ARCHITECT i System	Different
Test Result Reporting	Reactive, Non-reactive and S/CO	Reactive, Non-reactive and S/CO	Similar
Imprecision	The assay was designed to have within-laboratory imprecision as listed below: • ≤ 0.100 S/CO SD for samples with S/CO < 1.00 • ≤ 10.0% CV for samples with S/CO ≥ 1.00	Within-Laboratory (Total) CV of ≤ 10% for positive controls and for reactive samples with S/CO ≤ 4, and a Within-Laboratory (Total) CV of ≤ 15% for samples with S/CO >4.	Different
Time to Result	~ 30 minutes	~ 29 minutes	Similar
Reagent Storage and Stability	Unopened at 2 to 10°C up to stated expiration date	Unopened at 2 to 8°C up to stated expiration date	Similar
Reagent On-board Stability	56 Days	30 days	Different
Calibration Frequency	56 Days	30 days	Different
Calibrator Open Vial	180 Days	When stored and handled as directed, the calibrator is stable until the expiration date.	Different
Control Levels	5 Levels (1 Negative and 4 Positive for Analyte Measured)	5 Levels (1 Negative and 4 Positive for Analyte Measured)	Similar
Control Matrix	QC1, 2,4 &5 = Human serum based QC3 = Buffer & protein based	Negative QC, QC1, 2,4 = Human serum based QC3 = Buffer & protein based	Similar
Control Open Vial	90 Days	When stored and handled as directed, the controls are stable until the expiration date.	Different

Summary of Studies

Within-Laboratory Imprecision

The imprecision/reproducibility of the Access HIV Ag/Ab combo assay was evaluated in a study based on CLSI guidance EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures*. A sixteen-member panel of patient samples for HIV antibody and an eight-member panel of patient samples for HIV antigen, including serum (S), plasma (P), and Access HIV Ag/Ab combo QC samples were assayed in duplicate in two runs per day over a minimum of 20 days. Three lots of Access HIV Ag/Ab combo reagent and calibrator were tested on three DxI 9000 Access Immunoassay Analyzers for the study (one lot per instrument). The combined results for all three lots are presented in the following within-laboratory imprecision tables.

HIV Antibody Within-Laboratory Imprecision

				Between Lot & Instrument		Between-Day		Between-Run		Within-Run		Within-Laboratory (Total)	
Sample	Analyte	N	Mean S/CO	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV
QC1	None	240	0.05	0.009	N/A	0.000	N/A	0.007	N/A	0.004	N/A	0.013	N/A
QC2	HIV-1 Ab	240	2.68	0.125	4.7	0.045	1.7	0.055	2.0	0.053	2.0	0.153	5.7
QC4	HIV-2 Ab	240	2.54	0.288	11.3	0.038	1.5	0.067	2.6	0.058	2.3	0.304	11.9
QC5	HIV-1O Ab	240	3.53	0.656	18.6	0.089	2.5	0.070	2.0	0.073	2.1	0.670	19.0
S1	None	240	0.05	0.009	N/A	0.002	N/A	0.007	N/A	0.004	N/A	0.012	N/A
S2	HIV-1M Ab	240	0.77	0.019	2.5	0.012	1.6	0.016	2.1	0.017	2.3	0.032	4.2
S4	HIV-1M Ab	240	1.18	0.035	2.9	0.019	1.6	0.029	2.5	0.024	2.0	0.055	4.6
S5	HIV-1M Ab	240	3.46	0.122	3.5	0.060	1.7	0.061	1.8	0.075	2.2	0.167	4.8
P1	HIV-1M Ab	240	0.80	0.024	3.0	0.018	2.2	0.016	2.0	0.017	2.1	0.038	4.7
P3	HIV-1M Ab	240	1.10	0.033	2.9	0.018	1.7	0.025	2.3	0.026	2.3	0.052	4.7
S6	HIV-1O Ab	240	1.17	0.119	10.2	0.017	1.5	0.026	2.2	0.024	2.0	0.125	10.7
S7	HIV-1O Ab	240	3.25	0.161	5.0	0.047	1.5	0.068	2.1	0.074	2.3	0.195	6.0
P4	HIV-1O Ab	240	1.24	0.098	7.9	0.022	1.8	0.030	2.4	0.025	2.0	0.108	8.7
S8	HIV-2 Ab	240	1.22	0.102	8.4	0.013	1.1	0.038	3.1	0.035	2.9	0.115	9.4
S9	HIV-2 Ab	240	3.41	0.238	7.0	0.084	2.5	0.074	2.2	0.094	2.7	0.279	8.2
P5	HIV-2 Ab	240	1.26	0.091	7.2	0.027	2.1	0.027	2.2	0.033	2.6	0.104	8.2

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.

HIV-1 p24 Antigen Within-Laboratory Imprecision

				Between Lot & Instrument		Between-Day		Between-Run		Within-Run		Within-Laboratory (Total)	
Sample	Analyte	N	Mean S/CO	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV
P2	HIV-1 p24	240	0.91	0.043	4.7	0.012	1.4	0.013	1.4	0.014	1.6	0.049	5.4
P6	HIV-1 p24	240	1.24	0.059	4.8	0.016	1.3	0.021	1.7	0.027	2.1	0.070	5.7
QC1	None	240	0.14	0.012	N/A	0.007	N/A	0.003	N/A	0.009	N/A	0.017	N/A
QC3	HIV-1p24	240	3.07	0.078	2.5	0.054	1.7	0.044	1.4	0.038	1.2	0.111	3.6
S1	None	240	0.16	0.013	N/A	0.005	N/A	0.005	N/A	0.007	N/A	0.016	N/A
S10	HIV-1 p24	240	1.12	0.047	4.2	0.015	1.4	0.018	1.7	0.017	1.5	0.056	5.0
S11	HIV-1 p24	240	3.83	0.186	4.9	0.045	1.2	0.061	1.6	0.060	1.6	0.210	5.5
S3	HIV-1 p24	240	0.83	0.043	5.2	0.016	2.0	0.012	1.4	0.018	2.2	0.051	6.1

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.

Another study was performed to estimate variance components for the Access HIV Ag/Ab combo assay including instrument, reagent lots, between-day, between-run and within-run, using three instruments and three reagent lots. Overall variance by analyte for Access HIV Ag/Ab combo is within the expected reproducibility performance of the assay. The HIV Ag analysis variance was assessed across three reagent pack lots, over three days and two runs per day. For HIV Ab analysis variance was assessed across three reagent pack lots, over six days, with one run per day.

HIV Antibody Variance

Sample ID	Analyte	Mean S/CO	n	CV or SD Instrument (S/CO)	CV or SD Reagent Lot (S/CO)	CV or SD Reproducibility (S/CO)
QC1 Lot1	None	0.062	162	0.006	0.011	0.017
QC1 Lot2	None	0.057	161	0.005	0.009	0.015
QC1 Lot3	None	0.065	162	0.006	0.010	0.018
QC2 Lot1	HIV-1 M	2.823	162	2.0%	3.7%	5.5%
QC2 Lot2	HIV-1 M	2.832	162	2.3%	3.7%	6.2%
QC2 Lot3	HIV-1 M	3.068	161	1.6%	1.3%	5.7%
QC4 Lot1	HIV-2	2.606	162	3.1%	7.1%	8.9%
QC4 Lot2	HIV-2	2.740	162	2.6%	6.9%	8.6%
QC4 Lot3	HIV-2	2.798	162	2.0%	7.0%	8.2%
QC5 Lot1	HIV-1 O	3.491	162	2.2%	11.8%	12.8%
QC5 Lot2	HIV-1 O	3.493	162	2.0%	11.7%	12.5%
QC5 Lot3	HIV-1 O	3.750	162	1.8%	12.7%	13.5%
P3	HIV-1 M	1.199	162	1.4%	2.4%	5.7%
P4	HIV-1 O	1.313	162	1.9%	4.7%	6.1%
P5	HIV-2	1.333	162	3.7%	3.0%	6.9%
P7	HIV-1 M	3.848	162	2.5%	2.8%	5.3%
P8	HIV-1 M	10.359	162	2.2%	3.0%	5.1%
S1	None	0.067	162	0.006	0.010	0.017
S12	HIV-1 M	39.089	162	1.8%	3.2%	5.4%
S13	HIV-1 M	132.268	162	2.4%	3.2%	5.4%
S14	HIV-1 M	197.292	162	2.7%	3.7%	5.7%
S15	None	0.064	162	0.004	0.010	0.015
S2	HIV-1 M	0.832	162	0.013	0.012	0.047
S4	HIV-1 M	1.267	161	2.7%	2.8%	6.4%
S5	HIV-1 M	5.760	162	3.3%	5.4%	7.3%
S6	HIV-1 O	1.239	162	1.1%	6.2%	7.2%
S7	HIV-1 O	10.769	161	2.3%	5.6%	7.1%
S8	HIV-2	1.279	162	3.3%	4.4%	7.5%
S9	HIV-2	7.592	161	4.3%	5.2%	8.5%

HIV-1 p24 Antigen Variance

Sample ID	Analyte	Mean S/CO	n	CV or SD Instrument (S/CO)	CV or SD Reagent Lot (S/CO)	CV or SD Reproducibility (S/CO)
PS1	None	0.163	162	0.004	0.010	0.013
QC1 Lot1	None	0.150	162	0.004	0.011	0.013
QC1 Lot2	None	0.151	162	0.004	0.011	0.014
QC1 Lot3	None	0.161	162	0.005	0.010	0.013
S15	None	0.154	162	0.003	0.011	0.014
P6	p24 Ag	1.284	161	1.5%	2.6%	4.3%
PS18	p24 Ag	4.543	162	0.6%	3.4%	4.4%
S10	p24 Ag	1.160	162	1.4%	2.2%	4.0%
S16	p24 Ag	144.418	162	1.3%	1.7%	3.9%
S3	p24 Ag	0.865	161	0.009	0.029	0.042
QC3 Lot1	p24 Ag	3.003	162	1.1%	2.1%	3.7%
QC3 Lot2	p24 Ag	3.040	162	1.5%	2.4%	4.7%
QC3 Lot3	p24 Ag	3.078	162	0.9%	2.1%	4.0%

Reproducibility

A 5-day reproducibility study was performed on the DxI 9000 Access Immunoassay analyzer based on CLSI guideline EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures*. A sixteen-member panel of patient samples for HIV antibody and an eight-member panel of patient samples for HIV antigen, including serum (S), plasma (P), and Access HIV Ag/Ab combo QC samples were assayed on three instruments at three different clinical sites, using one lot of Access HIV Ag/Ab combo reagent and calibrator. Each panel member was assayed in replicates of three at two separate times per day.

HIV Antibody Reproducibility

			Between-Site		Between-Day		Between-Run		Repeatability (Within-Run)		Reproducibility	
Sample	N	Mean (S/CO)	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV
S1	90	0.06	0.003	N/A	0.004	N/A	0.001	N/A	0.005	N/A	0.007	N/A
S2	90	0.86	0.062	7.2	0.000	0.0	0.019	2.2	0.022	2.6	0.068	8.0
S4	90	1.30	0.097	7.4	0.000	0.0	0.015	1.2	0.036	2.7	0.105	8.0
S5	90	3.84	0.249	6.5	0.054	1.4	0.073	1.9	0.104	2.7	0.285	7.4
S6	90	1.39	0.114	8.2	0.000	0.0	0.021	1.5	0.030	2.2	0.120	8.6
S7	90	3.57	0.272	7.6	0.027	0.7	0.029	0.8	0.070	2.0	0.283	7.9
S8	90	1.39	0.108	7.8	0.028	2.0	0.035	2.5	0.048	3.5	0.127	9.1
S9	90	3.84	0.338	8.8	0.093	2.4	0.050	1.3	0.126	3.3	0.376	9.8
P1	90	0.85	0.059	6.9	0.013	1.5	0.013	1.5	0.022	2.6	0.065	7.7
P3	90	1.20	0.090	7.5	0.023	1.9	0.024	2.0	0.038	3.1	0.103	8.5
P4	90	1.21	0.081	6.7	0.012	1.0	0.016	1.4	0.035	2.9	0.090	7.5
P5	90	1.06	0.101	9.5	0.022	2.1	0.011	1.0	0.040	3.8	0.111	10.5
QC1 (negative)	90	0.05	0.002	N/A	0.001	N/A	0.000	N/A	0.010	N/A	0.010	N/A
QC2 (HIV-1 Ab)	90	3.15	0.201	6.4	0.074	2.3	0.000	0.0	0.093	2.9	0.234	7.4
QC4 (HIV-2 Ab)	90	3.17	0.251	7.9	0.000	0.0	0.133	4.2	0.147	4.6	0.320	10.1
QC5 (HIV-1 group O Ab)	90	4.63	0.324	7.0	0.104	2.2	0.120	2.6	0.158	3.4	0.394	8.5

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.

HIV-1 p24 Antigen Reproducibility

			Between-Site		Between-Day		Between-Run		Repeatability (Within-Run)		Reproducibility	
Sample	N	Mean (S/CO)	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV	SD (S/CO)	%CV
S1	90	0.17	0.002	N/A	0.003	N/A	0.005	N/A	0.010	N/A	0.012	N/A
S3	90	0.85	0.008	0.9	0.011	1.3	0.013	1.6	0.016	1.9	0.025	2.9
S10	90	1.12	0.022	2.0	0.010	0.9	0.015	1.3	0.019	1.7	0.034	3.0
S11	90	3.79	0.085	2.2	0.000	0.0	0.049	1.3	0.059	1.6	0.114	3.0
P2	90	0.97	0.017	1.7	0.016	1.6	0.006	0.6	0.018	1.9	0.030	3.1
P6	90	1.24	0.026	2.1	0.014	1.1	0.012	1.0	0.024	1.9	0.040	3.2
QC1 (negative)	90	0.16	0.000	N/A	0.002	N/A	0.000	N/A	0.010	N/A	0.010	N/A
QC3 (HIV-1 p24 Ag)	90	3.02	0.031	1.0	0.000	0.0	0.030	1.0	0.051	1.7	0.067	2.2

Note: %CV are not meaningful when S/CO approaches zero. Results are noted as N/A.

Limit of Blank (LoB) and Limit of Detection (LoD)
LoB and LoD studies were conducted on the DxI 9000 Access Immunoassay Analyzer following methods described in CLSI guideline EP17-A2:2012, *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*. LoB was calculated separately for two reagent lots for both serum and plasma using the non-parametric method. The maximum LoB estimates were carried forward in the Limit of Detection (LoD) calculation where precision profile models relating standard deviation and mean S/CO for each sample and reagent lot were used to estimate the LoD. The maximum observed LoB and LoD results for both HIV-1 p24 antigen and HIV antibody are shown in the following table:

	Limit of Blank (LoB) S/CO	**Limit of Detection (LoD) S/CO**
HIV-1 p24 antigen (serum)	0.28	0.30
HIV-1 p24 antigen (plasma)	0.18	0.19
HIV antibody (serum)	0.08	0.10
HIV antibody (plasma)	0.11	0.13

Matrix Comparison
A matrix comparison study established the equivalence of serum and plasma specimens using the Access HIV Ag/Ab combo assay on the DxI 9000 Access Immunoassay Analyzer. The study was performed using a protocol based on CLSI guideline EP09C, 3rd Edition, *Method Comparison and Bias Estimation Using Patient Samples*. Matched donor sets consisting of nine specimen types each were evaluated. Fifty samples were evaluated with the HIV Ag assessment for each sample type. Fifty-three samples were evaluated with the HIV Ab assessment for each sample type. Serum served as the reference tube type. A Passing-Bablok regression analysis (using the mean test sample results versus the mean reference results) was completed for each matrix to determine the regression equation, slope with bootstrap 95% confidence intervals, and the correlation coefficient (r).

The Access HIV Ag/Ab combo assay demonstrated sample type equivalence between serum (no gel) and eight serum/plasma matrices. Passing Bablok regression slopes ranged from 0.90 to 1.00 for the HIV Ag assessment and 0.98 to 1.04 for the HIV Ab assessment.

The Access HIV Ag/Ab combo assay detects HIV Ag and Ab in the following matrices.

Sample Type
Serum (Reference)
Serum Separator Tube
Plasma Lithium Heparin
Plasma Lithium Heparin Separator Tube
Plasma K_2 EDTA
Plasma K_3 EDTA
Plasma Sodium Citrate
Plasma Acid Citrate Dextrose (ACD)
Plasma Citrate Phosphate Dextrose (CPD)

Sample Stability

Sample Handling Stability

Sample handling and freeze/thaw stability was established for the Access HIV Ag/Ab combo assay on the DxI 9000 Access Immunoassay Analyzer. The study is based on CLSI guideline GP44-A4, *Procedures for the Handling and Processing of Blood* & CLSI guideline EP25-A. *Evaluation of Stability of In Vitro Diagnostic Reagents*. The mean S/CO bias for stressed vs. unstressed samples was within ± 0.150 for negative samples, and the mean S/CO percentage bias for stressed vs. unstressed samples was within ± 15.0% for positive samples. The study verified the following sample handling claims:

72 hours at 20-25°C,
7 days at 2-8°C,
30 days at ≤ -20°C,
and up to 5 Freeze/Thaw cycles.

Fresh vs Frozen Sample Stability

A fresh vs frozen sample equivalency study was also performed to evaluate the equivalency between fresh samples (never frozen) and frozen samples after storage at ≤ -18°C for at least 16 hours with the Access HIV Ag/Ab combo assay on the DxI 9000 Access Immunoassay Analyzer.

Fresh and frozen samples demonstrated equivalency using the Access HIV Ag/Ab combo assay.

Fresh vs Frozen Samples Regression Analysis Results

	n	All Samples Combined Slope	n	Reactive Samples Slope
Ag	46	1.00	31	0.99
Ab	51	1.00	34	1.01

Reagent Stability

Reagent Shelf-life

Access HIV Ag/Ab combo shelf-life dating was established based on real time stability (RTS) studies for the Access HIV Ag/Ab combo reagent pack. The study was performed to verify the stability at the recommended storage condition (2-10°C), using a protocol based on CLSI guideline EP25-A. The study also included evaluation of reagent pack stability following simulated winter and summer transport stresses of the reagent packs.

The results from the Access HIV Ag/Ab combo reagent pack shelf-life study show that the packs are stable for 365 days at the recommended storage condition of 2-10°C.

Reagent In-use Stability (Open Pack)

Reagent open pack stability of the Access HIV Ag/Ab combo assay was evaluated at the recommended open storage conditions (2-10°C) using a protocol based on CLSI guideline EP25-A. The study also included evaluation of open pack stability following simulated winter and summer transport stresses of the reagent packs.

The Access HIV Ag/Ab combo reagent pack is stable after opening for up to 56 days when stored at 2-10°C.

Stored Curve Calibration Stability
Access HIV Ag/Ab combo assay stored curve calibration stability was verified on the DxI 9000 Access Immunoassay Analyzer. The evaluation was performed using a protocol based on CLSI guideline EP25-A. The study also included evaluation of calibration stability following simulated winter and summer transport stresses of the reagent packs.

Access HIV Ag/Ab combo stored calibration stability is 56 days.

Calibrator Stability
Calibrator Shelf-life
Access HIV Ag/Ab combo Calibrators shelf-life dating was established based on real time stability (RTS) studies for the Access HIV Ag/Ab combo Calibrators. The study was performed to verify stability at the recommended storage condition (2-10°C), using a protocol based on CLSI guideline EP25-A. The study also included evaluation of calibrator stability following simulated winter and summer transport stresses of the vials.

The final shelf-life dating for the Access HIV Ag/Ab combo Calibrators is 298 days, which reflects the minimum achieved stability duration across the three lots tested.

Calibrator In-use Stability (Open Vial)
Open vial stability of the Access HIV Ag/Ab combo Calibrators on the DxI 9000 Access Immunoassay Analyzer was evaluated at the recommended open vial storage conditions (2-10°C) using a protocol based on CLSI guideline EP25-A. The study also included evaluation of calibrator open vial stability following simulated winter and summer transport stresses of the vials.

Access HIV Ag/Ab combo Calibrators are stable when stored at 2-10°C for 180 days after initial use.

QC Stability
QC Shelf-life
Access HIV Ag/Ab combo QC shelf-life dating was established based on real time stability (RTS) studies for the Access HIV Ag/Ab combo QC (QC1 – QC5). The study was performed to verify the stability at the recommended storage condition (2-10°C), using a protocol based on CLSI guideline EP25-A. The study also included evaluation of QC stability following simulated winter and summer transport stresses of the vials.

The final shelf-life dating for the Access HIV Ag/Ab combo QC is 339 days, which reflects the minimum achieved stability duration across the three lots tested.

QC In-use Stability (Open Vial)
Open vial stability of the Access HIV Ag/Ab combo QC on the DxI 9000 Access Immunoassay Analyzer was evaluated at the recommended open vial storage conditions (2-10°C) using a protocol based on CLSI guideline EP25-A. The study also included evaluation of QC open vial stability following simulated winter and summer transport stresses of the vials.

The Access HIV Ag/Ab combo QC are stable when stored at 2-10°C for 90 days after initial use.

Analytical Sensitivity

Antigen Detection

The analytical sensitivity of the Access HIV Ag/Ab combo assay for HIV-1 p24 antigen was designed to be less than or equal to 2.00 IU/mL using the WHO International Standard HIV-1 p24 Antigen NIBSC (National Institute for Biological Standards and Controls) code: 90/636.

To examine the analytical sensitivity of the Access HIV Ag/Ab combo assay on the DxI 9000 Access Immunoassay Analyzer, a series of dilutions was prepared in serum and plasma samples using the WHO IS 90/636 to target HIV-1 p24 antigen concentrations in the range of 0.10 – 1.00 IU/mL. The dilutions were assayed using three reagent pack lots and three calibrator lots on two DxI 9000 Access Immunoassay analyzers over three days. The analytical sensitivity for each reagent/calibrator lot combination was determined using a linear fit regression of the S/CO versus the WHO IS 90/636 concentrations (IU/mL). The point estimate of the WHO IS concentration corresponding to S/CO = 1.00 and the 95% CI were used in the analytical sensitivity estimation. The maximum overall analytical sensitivity result determined in this study is summarized in the following table:

Standard	Analytical Sensitivity
WHO International Standard HIV-1 p24 Antigen NIBSC code: 90/636.	0.22 IU/mL (1.66 pg/mL*)

*Conversion from IU/mL to pg/mL of HIV-1 p24 Ag using WHO calibration curve tested on VIDAS® HIV p24 II assay. VIDAS® is a registered trademark of bioMérieux, SA.

Antibody Detection

There is no internationally recognized standard for HIV-1 or HIV-2 specific antibody.

Intra-Assay Carryover

Testing was conducted to assess the HIV antigen (Ag) and HIV antibody (Ab) sample-to-sample and sample-to-reagent pack carryover on the Access HIV Ag/Ab combo assay. Test procedures were based on the guidance document, CLSI guideline EP10-A3, *Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures*.

No intra-assay carryover was observed with the Access HIV Ag/Ab combo assay tested on the DxI 9000 Access Immunoassay Analyzer.

Hook Effect

A hook study was performed to evaluate whether high levels of analyte in patient specimens result in a hook effect that changes the reported results of the Access HIV Ag/Ab combo assay on the DxI 9000 Access Immunoassay Analyzer.

For the HIV antibody assessment, there were no changes to the interpretation of the results on three reagent pack lots. For the HIV-1 p24 antigen assessment (up to 1 µg/mL), there were no changes to the interpretation of the results, on three reagent pack lots.

No false negative results due to high-dose hook effect were observed with the Access HIV Ag/Ab combo assay.

Interfering Substances

The Access HIV Ag/Ab combo assay was evaluated for interference consistent with CLSI guideline EP07 3rd Edition, *Interference Testing in Clinical Chemistry*. Testing was performed using serum samples containing high negative and low positive levels of HIV-1 p24 antigen and HIV-1 antibodies, spiked with potential interferents, at the concentrations indicated. Of the compounds tested, none were found to cause significant interference using the highest test concentrations indicated in the following table.

Potential Interferent	Highest Concentration Added
Hemoglobin	500 mg/dL
Total Protein	15 g/dL
Gamma Globulin	20 g/L
Bilirubin conjugated	43 mg/dL
Bilirubin unconjugated	43 mg/dL
Triglycerides Intralipid	2,000 mg/dL
Biotin	3,510 ng/mL
Aspirin (Acetylsalicylic Acid)	167 µmol/L
Salicylic Acid	207 µmol/L
Acetaminophen (Paracetamol)	1,030 µmol/L
Ibuprofen	1,060 µmol/L
Atorvastatin	1.34 µmol/L
Lisinopril	0.607 µmol/L
Levothyroxine	0.552 µmol/L
Metformin	92.9 µmol/L
Amlodipine	0.183 µmol/L
Omeprazole	24.3 µmol/L
Sertraline	3.03 µmol/L

Cross Reactivity

Cross-reactivity was evaluated by testing 290 samples for potentially cross-reacting conditions. For preparation of bacterial samples, negative samples were spiked with bacteria (10^5 CFU/mL) prior to evaluation. No cross-reactivity was observed. The results are summarized in the following table:

Category	Number of samples tested	Number of reactive samples	Number of nonreactive samples
Epstein-Barr virus (EBV)	10	0	10
Cytomegalovirus (CMV)	10	0	10
Herpes simplex virus (HSV1/2)	10	0	10
Varicella-zoster virus (VZV)	10	0	10
Human T-cell Lymphotropic Virus (HTLV I & II)	10	0	10
Hepatitis A Virus (HAV)	10	0	10
Hepatitis B Virus (HBV)	10	0	10
Hepatitis C virus (HCV)	10	0	10
Syphilis	10	0	10
Toxoplasmosis	10	0	10
anti-E. coli (including *E. coli* urinary infection)	10	0	10
Influenza post-vaccination	10	0	10
Rheumatoid Factor	10	0	10
HAMA	10	0	10
Anti-Nuclear Antibody (ANA)	10	0	10
Graves' Disease	10	0	10
Crohn's Disease	10	0	10
Pregnancy multiparous	10	0	10
Pregnancy first trimester	10	0	10
Pregnancy second trimester	10	0	10
Pregnancy third trimester	10	0	10
Transplant / Transplant recipient	10	0	10
Dialysis patients	10	0	10
Hemophiliac / Clotting factor	10	0	10
Systemic lupus erythematosus (SLE)	10	0	10
Influenza A virus	10	0	10
S. aureus	10	0	10
P. aeruginosa	10	0	10
E. coli	10	0	10
Total	**290**	**0**	**290**

Seroconversion

30 commercially available patient seroconversion panels were tested using the Access HIV Ag/Ab combo assay and a commercially available HIV Ag/Ab combo comparator assay to determine the seroconversion sensitivity of the assay. The Access HIV Ag/Ab combo assay detected HIV one to two bleeds earlier than the comparator assay in 11 of the 30 panels. Both assays exhibited equivalent detection with no difference in bleed number in 19 of the 30 panels. The results are summarized in the following table.

Panel ID	HIV Ag/Ab combo first reactive result from initial draw date		Access HIV Ag/Ab combo Assay vs Comparator assay
	Access HIV Ag/Ab combo assay (days)	Comparator assay (days)	Difference in bleed number of first reactive result*
0600-0227	7	7	0
0600-0232	18	18	0
0600-0237	3	7	-1
0600-0238	14	17	-1
0600-0240	47	47	0
0600-0244	14	14	0
0600-0245	14	17	-1
0600-0250	26	26	0
0600-0251	61	70	-2
0600-0258	7	9	-1
0600-0260	14	14	0
0600-0261	0	7	-2
0600-0262	13	13	0
0600-0265	28	28	0
0600-0271	3	7	-1
0600-0272	18	18	0
HIV6248	18	18	0
HIV9011	38	38	0
HIV9012	14	16	-1
HIV9013	23	25	-1
HIV9016	30	30	0
HIV9019	38	38	0
HIV9020	87	90	-1
HIV9021	47	47	0
HIV9023	78	78	0
HIV9028	53	53	0
HIV9030	47	47	0
HIV9031	138	146	-1
HIV9081	24	24	0
HIV9096	3	3	0

*The difference in bleed number is compared to the comparator assay. For example, -1 indicates that the comparator assay required 1 additional bleed before reactivity was determined compared to the Access HIV Ag/Ab combo assay.

Sensitivity in Antibody Positive non-B Subtype Samples
Sensitivity of the Access HIV Ag/Ab combo assay to detect 33 HIV-1 non-B subtypes (comprising HIV-1 group M subtypes and CRFs, as well as HIV-1 group O) was evaluated. A total of 311 samples were tested and 100% (311/311) were found reactive using the Access HIV Ag/Ab combo assay. The results are summarized in the following table:

HIV-1 Subtype, CRF, or Group	Number of Specimens	Number Reactive
A	5	5
A1	10	10
A2	4	4
C	20	20
D	16	16
F1	12	12
F2	5	5
G	14	14
H	10	10
J	3	3
K	1	1
cpx	21	21
CRF01	37	37
CRF02	75	75
CRF03	2	2
CRF04	1	1
CRF06	9	9
CRF07	1	1
CRF09	2	2
CRF11	11	11
CRF12	3	3
CRF13	5	5
CRF14	1	1
CRF18	7	7
CRF22	4	4
CRF25	3	3
CRF37	12	12
CRF43	2	2
CRF45	2	2
CRF49	1	1
CRF60	1	1
CRF94	1	1
HIV-1 group O	10	10
Total	**311**	**311**

Sensitivity to Detect Antigen Subtypes
Cell culture supernatants comprising different HIV-1 group M subtypes (A, B, C, D, F, G, H) and CRF-01, 02, 06, 11, 14, 15, 18 and 36 were evaluated with the Access HIV Ag/Ab combo assay. Supernatants from HIV-1 group O (including subtype H and T) and HIV-2 (subtype A and B) were also tested. Of the 50 total supernatants tested, 100% were found to be reactive using the Access HIV Ag/Ab combo assay.

HIV viral subtype, CRF or group	Number of samples	Number Repeatedly Reactive
HIV-1 group M - subtype A	4	4
HIV-1 group M - subtype B	7	7
HIV-1 group M - subtype C	4	4
HIV-1 group M - subtype D	4	4
HIV-1 group M - subtype F	3	3
HIV-1 group M - subtype G	4	4
HIV-1 group M - subtype H	1	1
CRF01	5	5
CRF02	4	4
CRF06	2	2
CRF11	1	1
CRF14	1	1
CRF15	1	1
CRF18	1	1
CRF36	1	1
HIV-1 group O	1	1
HIV-1 group O - subtype H	1	1
HIV-1 group O - subtype T	1	1
HIV-2 group A	2	2
HIV-2 group B	2	2
Total	**50**	**50**

Clinical Performance Evaluation

Study Overview
A multi-center study was conducted using the DxI 9000 Access Immunoassay Analyzer to evaluate the ability of the Access HIV Ag/Ab combo assay to detect HIV in specimens from the intended use population. This study enrolled adult, pediatric and pregnant subjects, primarily from the U.S., who were considered high risk, low risk, or known positive for HIV infection according to current Centers for Disease Control & Prevention (CDC) recommendations for the diagnosis of HIV infection. The overall study population included 10,254 samples (21.8% Plasma and 78.2% Serum) consisting of 9,079 (88.5%) that were prospectively collected, and an additional 1,175 (11.5%) pre-characterized retrospective samples collected from known positive HIV or high-risk patients.

Determination of Patient Infection Status (PIS)
Clinical sensitivity and specificity of the Access HIV Ag/Ab combo assay were evaluated on the DxI 9000 Access Immunoassay Analyzer compared to the final PIS determined following an algorithm aligned with current CDC recommendations for the diagnosis of HIV infection. All samples were tested with the Access HIV Ag/Ab combo assay and an FDA approved HIV Ag/Ab combo comparator assay. Samples found repeatedly reactive on the Access HIV Ag/Ab combo assay, or the comparator HIV Ag/Ab combo assay, were investigated further with confirmatory testing using an FDA approved HIV-1/2 differentiation assay (HIV assay with differentiation between HIV-1 and HIV-2) and/or an FDA approved HIV-1 RNA PCR assay as needed. Subjects with indeterminant final HIV PIS were not included in the analysis.

Clinical Specificity
A total of 7,156 subjects were tested in the low-risk population, including 6,259 low-risk adults, 408 low-risk pediatrics and 489 low-risk pregnant women. A total of 1,514 subjects were tested in the high-risk population, including 570 high-risk adults, 106 high-risk pediatrics, 146 high-risk pregnant women and 692 from HIV-2 endemic regions. The overall summary of the comparison of the Access HIV Ag/Ab combo assay and the comparator HIV Ag/Ab combo assay is shown in the following table.

Reactivity of Access HIV Ag/Ab Combo Assay Compared to the Comparator HIV Ag/Ab Combo Assay

Category		N Tested	Access HIV Ag/Ab combo assay			FDA approved HIV Ag/Ab combo comparator assay			Final HIV PIS	
			NR	IR	RR	NR	IR	RR	Positive	Negative
HIV Low Risk	Adults (non-pregnant)	6,259	6,060	201	199	6,007	280	252	174	6,085
	Pediatrics (non-pregnant)	408	407	1	1	404	6	4	1	407
	Pregnant	489	489	0	0	483	6	6	0	489
HIV High Risk	Adults (non-pregnant)	570	548	22	22	541	32	29	21	549
	Pediatrics (non-pregnant)	106	104	2	2	102	4	4	2	104
	Pregnant	146	146	0	0	145	3	1	0	146
HIV High Risk from HIV-2 endemic regions		692	685	7	7	686	6	6	5	687
Total		**8,670**	**8,439**	**233**	**231***	**8,368**	**337**	**302***	**203***	**8,467**

NR = nonreactive, IR = initially reactive, RR = repeatedly reactive, PIS = Patient Infection Status

*Both the Access HIV Ag/Ab combo assay and the comparator HIV Ag/Ab combo assay had samples that were repeat reactive but had a final negative HIV PIS.

Summary of Clinical Specificity Results

Cohort	Matrix	Clinical Specificity of the Access HIV Ag/Ab combo assay	
		% (n/N)	95% CI
HIV Low Risk	**All samples**	**99.6 (6,956/6,981)**	**99.5-99.8**
	Serum	99.7 (5,184/5,197)	99.6-99.9
	Plasma	99.3 (1,772/1,784)	98.8-99.6
HIV High Risk*	**All samples**	**99.8 (1,483/1,486)**	**99.4-99.9**
	Serum	99.8 (1,482/1,485)	99.4-99.9
	Plasma	100.0 (1/1)	20.7-100.0
Total	**All samples**	**99.7% (8,439/8,467)**	**99.5 - 99.8**

*Includes high-risk from HIV-2 endemic regions

Low Risk Cohort
A total of 7,156 samples from individuals at low risk for HIV were tested, of which 175 had a final HIV PIS of 'positive' and 6,981 had a final HIV PIS of "negative". Based on the data, 6,956/6,981 were nonreactive on the Access HIV Ag/Ab combo assay. Of the 25 subjects that were reactive on the Access HIV Ag/Ab combo assay and also had a final HIV PIS status of negative, 4 were also reactive on the comparator HIV Ag/Ab combo assay. Additionally, 1 subject that was also reactive on the comparator assay was HIV indeterminant on the HIV-1/2 differentiation assay.

High Risk Cohort
A total of 1,514 samples from individuals at high risk for HIV were tested, of which 28 had a final HIV PIS of 'positive' and 1,486 had a final HIV PIS of "negative". Based on the data, 1,483/1,486 were nonreactive on the Access HIV Ag/Ab combo assay. Of the 3 subjects that were reactive on the Access HIV Ag/Ab combo assay and also had a final HIV PIS status of negative, 2 were also reactive on the comparator HIV Ag/Ab combo assay. Additionally, 1 subject that was also reactive on the comparator assay was HIV indeterminant on the HIV-1/2 differentiation assay.

The overall specificity of the Access HIV Ag/Ab combo assay, for both low and high risk populations, was found to be 99.7% (8,439/8,467) with a 95th percentile confidence interval of 99.5% to 99.8%.

Clinical Sensitivity

Reactivity in Individuals Known to Be Positive for HIV
The clinical sensitivity of the Access HIV Ag/Ab combo assay in individuals known to be positive for HIV was determined using a total of 1,584 subjects and included 1,153 HIV-1 known positive adult subjects, 56 HIV-1 confirmed positive pediatric subjects, 48 HIV-1 confirmed positive pregnant subjects, 178 known HIV-2 positive subjects, 37 known HIV-1 group O positive samples, 80 HIV-1 group M positive samples and 32 HIV-1 p24 antigen known positive samples. An overall summary of the comparison of the Access HIV Ag/Ab combo assay compared to the FDA approved HIV Ag/Ab combo assay for all samples based on each subject cohort is shown in the following table.

Reactivity in Individuals Known to Be Positive for HIV

Category		N Tested	Access HIV Ag/Ab combo assay			FDA approved HIV Ag/Ab combo comparator assay			Final HIV PIS Positive
			NR	IR	RR	NR	IR	RR	
Known HIV-1 Positive	Adult (non-Pregnant)	1,153	0	1,153	1,153	0	1,153	1,153	1,153
	Pediatric (non-Pregnant)	56	0	56	56	0	56	56	56
	Pregnant	48	0	48	48	0	48	48	48
Known HIV-2 Positive	All Subjects	178	0	178	178	0	178	178	178
Known HIV -1 group O positive	All Subjects	37	0	37	37	0	37	37	37
Known HIV-1 group M positive	All Subjects	80	0	80	80	0	80	80	80
Known HIV-1 p24 antigen positive	All Subjects	32*	0	32	32	3	28	28	32
Total		**1,584**	**0**	**1,584**	**1,584**	**3**	**1,580**	**1,580**	**1,584**

NR = nonreactive, IR = initially reactive, RR = repeatedly reactive, PIS = Patient Infection Status

*The total N tested for known HIV-1 p24 antigen positive samples was 32 for the Access HIV Ag/Ab combo assay and 31 for the FDA approved comparator HIV Ag/Ab combo assay.

Comparison of the Clinical Sensitivity of the Access HIV Ag/Ab Combo Assay with an FDA Approved HIV Ag/Ab Combo Comparator Assay

The sensitivity of the Access HIV Ag/Ab combo assay in individuals known to be positive for HIV was determined using 1,584 samples. All samples (1,584/1,584) had a final HIV PIS status of "positive" resulting in a clinical sensitivity of 100% with a 95th percentile confidence interval of 99.8% to 100%.

Cohort		Access HIV Ag/Ab combo assay		FDA approved HIV Ag/Ab combo comparator assay	
		Clinical Sensitivity % (n/N)	95% CI	Clinical Sensitivity % (n/N)	95% CI
Known HIV-1 Positive	Adult (non-pregnant)	100.0 (1,153/1,153)	99.7-100.0	100.0 (1,153/1,153)	99.7-100.0
	Pediatric (non-Pregnant)	100.0 (56/56)	93.6-100.0	100.0 (56/56)	93.6-100.0
	Pregnant	100.0 (48/48)	92.6-100.0	100.0 (48/48)	92.6-100.0
Known HIV-2 Positive	All Subjects	100.0 (178/178)	97.9-100.0	100.0 (178/178)	97.9-100.0
Known HIV -1 group O positive	All Subjects	100.0 (37/37)	90.6-100.0	100.0 (37/37)	90.6-100.0
Known HIV-1 group M positive	All Subjects	100.0 (80/80)	95.4-100.0	100.0 (80/80)	95.4-100.0
Known HIV-1 p24 antigen positive	All Subjects	100.0 (32/32)*	89.3-100.0	90.3 (28/31)*	75.1-96.7
Total		**100.0 (1,584/1,584)**	**99.8-100.0**	**99.8 (1,580/1,583)**	**99.4-99.9**

*The total N tested for known HIV-1 p24 antigen positive samples was 32 for the Access HIV Ag/Ab combo assay (all confirmed PIS positive) and 31 for the FDA approved HIV Ag/Ab combo comparator assay (all confirmed PIS positive).

Sensitivity of All Subjects Positive for HIV

The overall clinical sensitivity of the Access HIV Ag/Ab combo assay on the DxI 9000 Access Immunoassay Analyzer was determined in 1,584 samples known to be positive for HIV-1 or HIV-2, plus 203 samples that were found to be positive from the low-risk and high-risk populations. All 1,787 samples had a final HIV PIS of "positive" for analysis.

Cohort	Matrix	Sensitivity	
		% (n/N)	95% CI
Subjects known positive for HIV	**All samples**	**100.0 (1,584/1,584)**	**99.8-100.0**
	Serum	100.0 (1,228/1,228)	99.7-100.0
	Plasma	100.0 (356/356)	98.9-100.0
All HIV positive samples	**All samples**	**100.0 (1,787/1,787)**	**99.8-100.0**
	Serum	100.0 (1,325/1,325)	99.7-100.0
	Plasma	100.0 (462/462)	99.2-100.0

The overall sensitivity of the Access HIV Ag/Ab combo assay was found to be 100.0% (1,787/1,787) with a 95th percentile confidence interval of 99.8% to 100.0%.

Reactivity in Individuals at High-Risk of HIV-1/2 Infection

The sensitivity of the Access HIV Ag/Ab combo in individuals at high risk for HIV was determined using a total of 1,514 subjects, including 570 adults, 106 pediatric subjects and 146 pregnant subjects, as well as an additional 692 subjects (524 adult and 168 pediatric) from an HIV-2 endemic area.

Category		N Tested	Access HIV Ag/Ab combo assay			FDA approved Ag/Ab combo comparator assay			Final HIV PIS Positive
			NR	IR	RR	NR	IR	RR	
High Risk n = 822	Adults (non-Pregnant)	570	548	22	22	541	32	29	21
	Pediatrics (non-Pregnant)	106	104	2	2	102	4	4	2
	Pregnant	146	146	0	0	145	3	1	0
High-risk HIV-2 from endemic regions n = 692	Adults (non-Pregnant)	524	517	7	7	518	6	6	5
	Pediatrics (non-Pregnant)	168	168	0	0	168	0	0	0
Total		**1,514**	**1,483**	**31**	**31**	**1,474**	**45**	**40**	**28**

NR = nonreactive, IR = initially reactive, RR = repeatedly reactive, PIS = Patient Infection Status

Of the total 1,514 subjects included in the sensitivity analysis, 28 subjects had a final HIV PIS of "positive". Five (5) of the 28 were collected from an HIV-2 endemic region. The final sensitivity of the Access HIV Ag/Ab combo assay for patients at high risk for HIV was 100% (28/28) with a 95th percentile confidence interval of 87.9% to 100%.

Reactivity in Pregnant Women

The clinical sensitivity of the Access HIV Ag/Ab combo assay in samples collected from pregnant women was determined using a total of 635 subjects and included 489 at low risk for HIV and 146 at high risk for HIV. A summary of the results of the Access HIV Ag/Ab combo assay and an FDA approved HIV Ag/Ab combo comparator assay for samples from pregnant women at low risk and high risk for HIV is shown in the following tables.

Low Risk Pregnant Cohort

Low-Risk Pregnant Women by Trimester	N Tested	Access HIV Ag/Ab combo assay			FDA approved HIV Ag/Ab combo comparator assay			Final HIV PIS positive
		NR	IR	RR	NR	IR	RR	
First	162	162	0	0	160	2	2	0
Second	168	168	0	0	166	2	2	0
Third	159	159	0	0	157	2	2	0
Total	**489**	**489**	**0**	**0**	**483**	**6**	**6**	**0**

NR = nonreactive, IR = initially reactive, RR = repeatedly reactive, PIS = Patient Infection Status

High Risk Pregnant Cohort

High-Risk Pregnant Women by Trimester	N Tested	Access HIV Ag/Ab combo assay			FDA approved HIV Ag/Ab combo comparator assay			Final HIV PIS positive
		NR	IR	RR	NR	IR	RR	
First	57	57	0	0	56	2	1	0
Second	43	43	0	0	43	0	0	0
Third	46	46	0	0	46	1	0	0
Total	**146**	**146**	**0**	**0**	**145**	**3**	**1**	**0**

NR = nonreactive, IR = initially reactive, RR = repeatedly reactive, PIS = Patient Infection Status

Reactivity in the Pediatric Population

The clinical sensitivity of the Access HIV Ag/Ab combo assay in pediatric individuals was determined using a total of 682 subjects and included 408 at low risk for HIV and 274 at high risk for HIV. A summary of the results of the Access HIV Ag/Ab combo assay and the comparator HIV Ag/Ab combo assay for low-risk and high-risk pediatric specimens is shown in the following tables.

Low Risk Pediatric Cohort
The clinical sensitivity of the Access HIV Ag/Ab combo assay in the low-risk pediatric population was found to be 100.0% (1/1) with a 95th percentile confidence interval of 20.7% to 100.0%.

Low-risk Pediatrics (years)	N Tested	Access HIV Ag/Ab combo assay			FDA approved HIV Ag/Ab combo comparator assay			Final HIV PIS positive
		NR	IR	RR	NR	IR	RR	
2-5	9	9	0	0	9	0	0	0
6-10	26	26	0	0	26	0	0	0
11-15	67	67	0	0	66	1	1	0
16-21	306	305	1	1	303	5	3	1

NR = nonreactive, IR = initially reactive, RR = repeatedly reactive, PIS = Patient Infection Status

High Risk Pediatric Cohort
The clinical sensitivity of the Access HIV Ag/Ab combo assay in the high-risk pediatric population was found to be 100.0% (2/2) with a 95th percentile confidence interval of 34.2% to 100.0%.

High-risk Pediatrics by Age (years)*	N Tested	Access HIV Ag/Ab combo assay			FDA approved HIV Ag/Ab combo comparator assay			Final HIV PIS positive
		NR	IR	RR	NR	IR	RR	
11-15	7	7	0	0	7	0	0	0
16-21	267	265	2	2	263	4	4	2

NR = nonreactive, IR = initially reactive, RR = repeatedly reactive, PIS = Patient Infection Status

*All results for high-risk pediatric subjects were for age groups greater than or equal to eleven years of age.

Substantial Equivalence Comparison Conclusion
The results of non-clinical analytical and clinical performance studies demonstrate that the Beckman Coulter Access HIV Ag/Ab combo assay for use on the DxI 9000 Access Immunoassay Analyzer is as safe, as effective, and performs as well as the predicate device.